REMARKS

I. PRELIMINARY REMARKS

Applicant thanks the Examiner for the Office Action of September 24, 2003, which has been studied with interest and care.

Claims 1, 8 and 17-23 were previously canceled, therefore Claims 2-7 and 9-16 remain pending in the instant application.

Rejection based on 35 USC 112, second paragraph, of Claims 2, 6 and 7 have been withdrawn. Further, amendments to Claims 2, 3, 5, 6, 7, 9, and 12 are not made for reasons of patentability; rather they are for reasons of clarity and to improve their form. For example, in Claims 2 and 9, the term "reagent" (line 6 and 7) has been changed to "binding moiety." Also, the term "binding moiety" is consistent with original claims 12 to 14. The term "binding moiety" narrows what type of "reagent" is contacting with the sample. Amendments to Claims 3, 5-7, and 12 are for reasons of correcting error in dependency of the claims. Claim 10 is cancelled because it was made redundant by Claims 2 and 9. Lastly, Claims 11 and 16 are cancelled. Thus, *no new subject matter* has been added to the claims and the changes made are to improve their form and definiteness as under 35 USC 112, second paragraph.

The non-statutory double patenting rejection is maintained for Claims 2, 6, 9, 10 and 12. Applicant notes that *a terminal disclaimer was mailed to the Office on July 9, 2003*. Copies of the transmittal letter, power of attorney, terminal disclaimer, and returned postcard are enclosed.

Hence, the following rejections under 35 USC 102(b) and 103(a) remain:

Claims 2-4 and 6 are rejected as being anticipated by Bianchi et al (WO 91/07660; or Bianchi).

Claims 2-4 and 6 are rejected as being anticipated by Spector et al (Am J Hum Genet. 32:79-87, 1980; or Spector).

Claims 5, 7, 9-12 and 14-16 are rejected as being unpatentable over Bianchi et al (WO 91/07660; or Bianchi), in view of Hume et al. (Early Hum. Dev. 42(2): 85-95, 1995; or Hume 1995) and Hume et al. (Blood 87(2): 762-770; or Hume).

Claim 13 is rejected as being unpatentable over Bianchi or Spector in view of Hume 1995 and Hume, as applied to claims 5, 7, 9-12 and 14-16, and further in view of Maggio (Immunoenzyme Technique I, CRC Press © 1980, pp. 186-187).

Therefore, Claims 2-7 and 9-16 are pending.

II. OBJECTION TO THE DRAWINGS

A formal drawing of Figure 1 is enclosed. The drawing complies with 37 CFR 1.84(b) for photographs.

III. REJECTIONS OF THE CLAIMS UNDER 35 USC 102

Applicant respectfully asserts that *not every element of every claim*, as amended, is taught by the references Bianchi or Spector. MPEP § 2131 provides:

> *A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference* (emphasis added)." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the ... claim." Richardson v. Suzuki Motor Co., 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). ...

Thus *each and every element* of the claimed invention has to be found in one reference, either Bianchi or Spector, in order that a 35 USC 102(b) rejection be properly maintained. Applicant respectfully asserts that Bianchi or Spector do not claim *each and every element* of the claimed invention as detailed below.

A. REJECTION OF CLAIMS 2-4 AND 6 AS ANTICIPATED UNDER 35 U.S.C. 102(b) BY *BIANCHI ET AL.*

Claims 2-4 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Bianchi et al. (WO 91/07660) (hereinafter, "Bianchi").

Bianchi described three potential routes for enriching a maternal blood sample for fetal cells.

1. Binding an antibody to an antigen on *maternal cells* and thereby removing the maternal cells from the sample (p. 10, line 21 through to p. 11, line 7; p. 27, line 12 through to p. 28, line 31).
2. Binding an antibody to an antigen present on *fetal cells*, and using this to enrich the sample (p. 11, line 15 through to p. 12, line 4; p. 29, line through to p. 30, line 19).
3. Both 1 and 2 above (p. 30, lines 20-30).

With regards to option two above, Bianchi discloses only the use of the transferrin receptor on fetal cells to enrich for fetal cells. In contrast, the claimed invention in Claim 2 step (c) explicitly recites that the claimed method requires that fetal or embryonic cells be isolated by virtue of their being bound to a moiety that binds a cell surface exposed adult liver component; but the adult liver component as claimed is not the transferrin receptor. Conversely, the transferrin receptor is not an adult liver component as disclosed by the claimed invention. The claimed invention discloses that a component of an adult liver cell is one, which is *predominantly associated* with the adult liver. However, if this "component is found in other tissues of the adult, it is either found at *low levels* in that other tissue compared to the liver or that the mass of the other tissue in which the said component is found, compared to the mass of the liver, is low so that the total amount of the adult liver component is higher in the whole liver compared to the total amount in the whole other tissue." Paragraph [0037]. Hence, the transferrin receptor is not an adult liver component as defined because it is found in a wide number of cells and tissues, with the *highest levels* found in erythroid cells (see p.9-10 of the response to the Office Action dated May 1, 2000, submitted to the Office on October 27, 2000 in the parent case). Lastly, the transferrin receptor is specifically *excluded* from the claimed invention.

The Office Action on page 12 (last line) stated that "the method is not limited to only transferrin receptor, therefore the rejection is maintained." However, absent any other teachings by Bianchi as to which other components can be used, one of ordinary skill in the art would not pursue cell surface exposed adult liver components as claimed. In fact, Bianchi only gives one

example and that is transferrin receptor. Bianchi does not give insight into which components may be used. Surface exposed adult liver components, but not the transferrin receptor, is exact subject matter of the claimed invention.

With regards to the Office Action's comments that Hle-1 (an anti-CD45 antibody) anticipates the claims. Applicant respectfully asserts that this is incorrect because Hle-1 binds to maternal cells, which is outside the scope of the claimed invention; which is for the purpose of binding fetal or embryonic cells (see amended Claim 2). Moreover, CD45 is also not an adult liver component as defined previously by the specification (see paragraph [0037] of the specification).

With regards to the Office Action's statement that the features relied upon for patentability are not recited in the claims (p.13, last paragraph of the Office Action). Applicant respectfully objects because the claims require that the fetal or embryonic cells are isolated by virtue of their being bound to a binding moiety that specifically binds an adult liver component on the cell surface of the fetal or embryonic cells. In short, the claimed invention binds fetal or embryonic cells and not maternal cells, using a binding moiety, which binds specifically to an adult liver component on the cell surface, which is not transferrin. As stated above, CD45 is not an adult liver component found on the cell surface; and further Bianchi uses CD45 to bind maternal cells and not fetal cells as recited in the claimed invention (see Claim 2 (c)).

Furthermore, the claimed invention copied the teachings of Bianchi (see paragraph [0017]) and the experiment was not successful; which is evidence that the teachings of Bianchi regarding the transferrin receptor do not result in a successful method of isolating fetal or embryonic cells. Hence, this aspect of the specification is not part of the claimed invention.

In summary, Bianchi does not disclose *each and every element* of the claimed invention as described above, therefore Bianchi does not anticipate the claimed invention.

B. REJECTION OF CLAIMS 2-4 AND 6 AS ANTICIPATED UNDER 35 U.S.C. 102(b) BY *SPECTOR ET AL*

Claims 2-4 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Spector et al. (Am J. Hum Genet. 32:79-87, 1980) (hereinafter, "Spector"). The Office Action contends that "*Spector* show[s] the identification and isolation of a specific adult liver component (Arginase)."

Applicant respectfully disagrees. Firstly, Spector teaches a method of analyzing fetal cells using the enzyme arginase as the marker. This is different from the claimed invention, which recites a method of isolating fetal cells by binding cell surface adult liver components. The claimed invention has nothing to do with *analyzing or assaying for the presence of arginase in fetal cells*. Secondly, because arginase is not a cell surface adult liver component as defined in the specification (see above discussion; and Paragraph [0007]), Spector does not anticipate Claim 2 . To clarify, arginase is a cytosolic enzyme and not a cell surface exposed component. Claim 2 recites that the adult liver component is a *cell surface exposed component*. Accordingly, arginase as disclosed in *Spector et al.* does not satisfy the requirements set out in the present claims, and *Spector et al.* therefore cannot anticipate the claims.

The Office Action also contends that arginase is present in the fetal stage of patients who would later develop arginase deficiency. Applicant respectfully argues that this is irrelevant and contradicted by Spector. On page 86, lines 3-6, Spector states that the diagnosis of fetal arginase deficiency could be made by a finding of a total absence of activity in fetal blood. However, even if the Office Action is correct that a fetus that would grow into an adult with arginase deficiency would express arginase during the fetal stage (although not true), arginase could not be considered to be an adult liver component for that individual, and hence would fall outside of the scope of the claimed invention (see claim 2).

In summary, Spector does not disclose *each and every element* of the claimed invention as described above; therefore Spector does not anticipate the claimed invention.

C. REJECTION OF CLAIMS 5, 7, 9-12, AND 14-16 AS OBVIOUS UNDER 35 U.S.C. 103(a)

Claims 5, 7, 9-12, and 14-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bianchi or Spector in view of Hume et al. (*Early Human Development*, Vol. 42, No. 2, 1995, pp. 85-95) (hereinafter, "Hume 1995"), and Hume et al. (*Blood*, Vol. 871, No. 2, 1996, pp. 762-770) (hereinafter, "Hume 1996").

Applicant respectfully argues that the cited prior art combinations are not proper on several grounds. Firstly, MPEP § 2143.01 states that there must be some *suggestion or motivation*, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify or combine reference teachings. Further, the Federal Circuit has produced a number of decisions overturning obviousness rejections due to a lack of suggestion in the prior art of the desirability of combining references, as discussed in the aforementioned section.

Secondly, MPEP 2141.04(a) states that the prior art has to be either be *in the field of the applicant's endeavor* or, if not, then be *reasonable pertinent to the particular problem* with which the inventor was concerned. *In re Oetiker*, 977 F.2d 1443, 1446. Further, "[a] reference is reasonably pertinent if, even though it may be in a different field from that of the inventor's endeavor, it is one which, because of the matter with which it deals, logically would have commended itself to an inventor's attention in considering his problem." *Wang Laboratories Inc., v. Toshiba Corp.*, 993 F.2d 858.

Lastly, the Office Action improperly applies the `obvious to try' standard in rejecting the claims.

The following is a detailed discussion of the above.

1. The prior art references teach away from the claimed invention.

Bianchi or Spector and in view of both Hume references teach away and do not suggest the claimed invention. As stated above, Bianchi teaches the use of the transferrin receptor to isolate fetal cells. However, the claimed invention specifically recites that the transferrin receptor should not be used, rather some other adult liver cell-surface component (see amended claim 2). One of ordinary skill in the art would not extrapolate the sole use of transferrin in

Bianchi to the claimed invention when in fact the claimed invention specifically states not to use the transferrin receptor. Therefore, Bianchi teaches away from the claimed invention because it only teaches the use of the transferrin receptor to isolate fetal cells.

Also stated above, Spector teaches a method of analyzing fetal cells using the enzyme arginase as the marker, rather than isolating fetal cells, as is a subject matter of the claimed invention. Further, arginase is a soluble cytosolic protein, rather than a cell surface adult liver component as defined in the specification (see above discussion; and Paragraph [0037]). One of ordinary skill in the art would not extrapolate the analysis of a cytosolic protein (arginase) as taught by Spector, to isolate fetal cells using a reagent which binds to a cell-surface adult liver component, as defined the claimed invention. Therefore, Spector teaches away from the claimed invention because it only teaches a method of analyzing fetal cells for the presence of arginase.

The Hume references disclose methods, which can be performed once fetal cells have been isolated, rather than a method of first isolating fetal cells by using a moiety, which binds to an adult liver cell surface component as in the claimed invention. Thus, the Hume references teach away from the claimed invention because the Hume references do not relate to isolation of fetal cells.

Accordingly, the combination of Bianchi in view of the Hume reference or Spector in view of the Hume references is improper, as all references teach away from the claimed invention. In summary, Bianchi teaches the use of transferrin to isolate fetal cells, Spector teaches methods of analyzing fetal cells by testing for the marker enzyme arginase, and the Hume references teach methods of analyzing fetal cells once they have been isolated. Hence, the primary and secondary references alone or combined do not teach the claimed invention, rather alone or combined they teach away the claimed invention.

2. The prior art references are not analogous to the claimed invention.

Secondly, the cited prior art references are not in the same field of the inventor's endeavor and are not properly combined. MPEP 2141.04(a) states that:

> In order to rely on the reference as a basis for rejection of the applicant's invention, the reference must either be in the field of

> the applicant's endeavor or, if not, then be reasonable pertinent to the particular problem with which the inventor was concerned. *In re Oetiker*, 977 F.2d 1443, 1446. A reference is reasonably pertinent if, even though it may be in a different field from that of the inventor's endeavor, it is one, which, because of the matter with which it deals, logically would have commended itself to an inventor's attention in considering his problem. *Wang Laboratories Inc., v. Toshiba Corp.*, 993 F.2d 858.

Briefly, Bianchi teaches the use of transferrin to isolate fetal cells, Spector teaches methods of analyzing fetal cells by testing for the marker enzyme arginase, and the Hume references teach methods of analyzing fetal cells once they have been isolated. Indeed, the Office Action states that Hume 1995 teaches that glucose-6-phosphatase is useful in *diagnosis* of disorders associated with liver protein expression, and not in a method of isolating fetal cells. Additionally, Applicant respectfully points out that it is well known to one of ordinary skill in the art that glucose-6-phosphatase is an intra-cellular (residing in the endoplasmic reticulum), and not cell-surface protein as alluded to by the Office Action. For example, Hume 1995, line 1 of the abstract, states glucose-6-phosphatase is "microsomal" – not cell surface. In another example, Hume 1995, on page 86, second paragraph, first line, states that "glucose-6-phosphatase is located in the endoplasmic reticulum." ER or cytosolic proteins are not cell surface proteins.

In summary, the combinations of references do not make obvious the claimed invention. First, the primary and secondary references are all non-analogous art and one of ordinary person skill in the art would not combine the aforementioned references. Thus, rendering the claimed invention unobvious. Secondly, even if Bianchi in view of both the Hume references were properly combined (or Spector in view of both Hume references), *which they are not*, they do not teach or suggest *all the limitations* of the claimed invention, which is required for an obviousness rejection. In fact, as stated above, Bianchi or Spector in view of the Hume references teaches away from the claimed invention.

3. The standard 'obvious to try' is improper if used to reject the claimed invention.

Lastly, Applicant respectfully asserts that the Office Action, although not specifically stating so in the Office Action, has improperly applied the standard of "obvious to try" to reject the claimed invention. MPEP 2141.04(a) states that it is improper to apply the 'obvious to try' standard' in at least two situations:

> [1]In some cases, what would have been `obvious to try' would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful....
> [2] In others, what was `obvious to try' was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it." *In re O'Farrell*, 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988) (citations omitted)

Both [1] and [2] apply to the instant application. With regards to [1], the prior art references of Bianchi or Spector in view of the Hume references "gave no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful." MPEP 2141.04(a). One of ordinary skill in the art in reviewing the above-cited references would not be compelled to:

(1) Use another cell surface adult liver component besides the transferrin receptor as taught in Bianchi. The use of another cell surface adult liver component to bind to fetal or embryonic cells is recited in the claimed invention (see amended claim 2), and not Bianchi. The claimed invention excludes the use of the transferrin receptor, thereby disregarding Bianchi.

(2) Isolate fetal or embryonic cells from the teachings of Spector; because Spector teaches an assay for *already* isolated fetal cells. Further, the use of a cytosolic or

soluble protein (i.e. arginase) is not a subject of the claimed invention; and even if it was tried, it would not lead to the claimed invention.

(3) Isolate fetal or embryonic cells from the teachings of the Hume references; because the Hume references do not teach methods of isolating fetal cells. Further, none of the proteins in the Hume references are cell surface proteins.

Thus, it is not "obvious to try" (1)-(3) to perform the claimed invention from the disclosures of the prior art because there is "no indication or direction" from the prior art to guide the ordinary person skilled in the art.

With regards to [2], it is also not obvious to try, "where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it," *In re O'Farrell*, 853 F.2d 894, 903, 7. For example, Bianchi discloses general teachings that a fetal-specific component could be used to isolate fetal cells (i.e. transferrin). In contrast, the claimed invention relates to specific examples of components that may be used (i.e. cell surface adult liver components). Similarly, Spector teaches analyzing fetal cells by looking for the marker enzyme arginase. Again, arginase is a cytosolic, soluble protein and does not guide a person of ordinary skill in the art to use a cell surface adult liver component to isolate fetal cells. Lastly, the Hume references perform assays to isolated cells rather than teach methods of isolating the same. So, no person with ordinary skill in the art would look to Hume for isolating fetal cells by binding them to a cell surface adult liver component.

Accordingly, with regards to both [1] and [2], the prior art references offer no guidance or direction and do not make it "obvious to try" to perform the claimed invention.

D. REJECTION OF CLAIM 13 AS OBVIOUS UNDER 35 U.S.C. 103(a)

Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bianchi or Spector in view of Hume et al. (*Early Human Development*, Vol. 42, No. 2, 1995, pp. 85-95) (hereinafter, "Hume 1995"), and Hume et al. (*Blood*, Vol. 871, No. 2, 1996, pp. 762-770)

(hereinafter, "Hume 1996"), and further in view of Maggio (Immunoenzyme Technique I, CRC Press © 1980, pp. 186-187).

Claim 13 is not obvious by virtue of its dependency on amended Claims 2 and 9, which as discussed above, are not anticipated by or obvious over the prior art references.

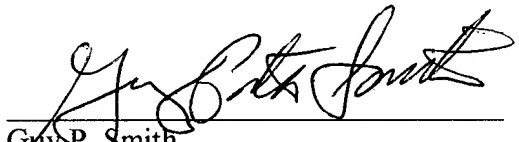
CONCLUSIONS

For the foregoing reasons, Applicant submits that all claims as currently presented are allowable over the prior art. The amendments made in this response are not for reasons of patentability, rather they are made for definiteness and clarity. Further, the amended claims do not add new subject matter.

If for any reason the Examiner finds the application other than in condition for allowance, Applicant encourages the Examiner to telephone Applicant's undersigned representative at 310-319-5414 to discuss the steps necessary for placing the application in condition for allowance. Applicant hereby authorizes the Commissioner to charge any additional fees, which may be required, or credit any overpayment to Deposit Account No. 16-2230.

Respectfully submitted,

Dated: January 23, 2004



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